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Anesthesiology
56:239, 1982

In reply: Pharmacokinetic analysis in anesthesia certainly has captured the interest of anesthesiologists as judged by the volume of correspondence arising from two recent thiopental pharmacokinetic publications,[1,2] and an accompanying editorial.[3] A goal of pharmacokinetic data analysis is to use the drug plasma concentration *vs.* time curve to characterize the rate of drug elimination from the body (clearance) and the extent of drug distribution (volume of distribution). These are often the most important parameters with physiologic meaning that can be obtained from plasma concentration *vs.* time data. As Dr. Feingold indicates, there are many mathematical techniques available to characterize the plasma concentration *vs.* time curve and derive the pharmacokinetic parameters of clearance and volume of distribution. Polyexponential equations have the advantages of being mathematically simple, not requiring complicated analytical techniques for fitting, and are used easily to calculate clearance and volume of distribution. There is a large body of experience in their application to pharmacokinetic data analysis.

Drs. Feingold and Mertens are bothered by the large intersubject variability in the thiopental pharmacokinetic parameters. This large variability may be due to the quality of data collection and analysis. It may, however, reflect the true large variability that exists in human populations. Large variability has been shown to be true for theophylline clearance in patients.[4] Large intersubject variability decreases the utility of the population mean as a predictor for any one individual, requires that group sizes be larger to demonstrate statistical differences between different populations, and emphasizes the need for individualization of drug dosage.

I would like to correct a graphical oversight in the editorial figure.[3] The intercept of the distribution phase (A) line should be below the predicted drug plasma concentration at time zero. This correction is shown in figure 1.

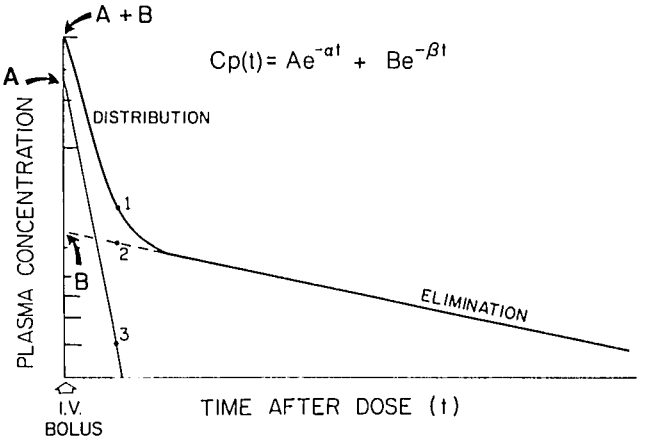

FIG. 1. To characterize the distribution phase it is necessary to subtract the concurrent and slower component of drug elimination. This is done by subtracting point 1 (plasma concentration observed on the distribution phase) from point 2 (corresponding plasma concentration on the extrapolated elimination phase line). The difference is plotted as a separate value, point 3. This feathering or residuals technique is done at several time intervals and a straight line drawn to characterize the residuals. The slope of this line represents the rate constant of the distribution phase (α).

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Another Warning Concerning the Hazards of Selector Shunt Values

To the Editor:—Hypoxic and barotrauma problems relating to the improper use of selector valves connecting ventilators to anesthesia gas machines continue to occur. Several reports of recent occurrences have been directed